· O H I O · W E S L E Y A N ·

Technical Report

ANALYSIS OF RETINAL FUNCTION FOLLOWING LASER IRRADIATION

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May 1990

DAMD17-88-C-8032

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SECURITY CLASSIFICATION OF THIS PAGE

REPORT DOCUMENTATION PAGE

Form Approved OMB No. 0704-0188

1a. REPORT SECURITY CLASSIFICATION: Unclassified	1b. RESTRICTIVE MARKINGS
2a. SECURITY CLASSIFICATION AUTHORITY	3. DISTRIBUTION/AVAILABILITY OF REPORT: Approved for public release; distribution unlimited
2b. DECLASSIFICATION/DOWNGRADING SCHEDULE	
4. PERFORMING ORGANIZATION REPORT NUMBER(S)	5. MONITORING ORGANIZATION REPORT NUMBER(S)
6a. NAME OF PERFORMING ORGANIZATION: Ohio Wesleyan University; 6b. OFFICE SYMBOL (If applicable)	7a. NAME OF MONITORING ORGANIZATION
6c. ADDRESS (City, State, and ZIP Code): Delaware, OH 43015	7b. ADDRESS (City, State, and ZIP Code)
8a. NAME OF FUNDING/SPONSORING ORGANIZATION: U.S. Army Medical Research and Development Command; 8b. OFFICE SYMBOL (If applicable)	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER: DAMD17-88-C-8032
8c. ADDRESS (City, State, and ZIP Code): Fort Detrick, Frederick, Maryland 21701-5012	10. SOURCE OF FUNDING NUMBERS: PROGRAM ELEMENT NO. 0602787A; PROJECT NO. 3E1-62787A878; TASK NO. BA; WORK UNIT ACCESSION NO. 209

11. TITLE (Include Security Classification): Analysis of Retinal Function Following Laser Irradiation

12. PERSONAL AUTHOR(S): David O. Robbins, Ph.D.

13a. TYPE OF REPORT	13b. TIME COVERED	14. DATE OF REPORT (Year, Month, Day)	15. PAGE COUNT
Midterm	FROM 10/30/87 TO 10/29/89	1990 May	23

16. SUPPLEMENTARY NOTATION

17. COSATI CODES		
FIELD	GROUP	SUB-GROUP
09	03	
20	06	

18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number): Laser safety (MPE), Nd/YAG, Rhesus monkeys, Flash effects (visual); Long-term visual deficits, light-induced damage, Glare effects.

19. ABSTRACT (Continue on reverse if necessary and identify by block number)

Exposure of the fovea to a single or multiple pulses of coherent light produce both transient and permanent changes in the eye's ability to resolve fine spatial detail. The immediate effects are often large, reflecting a total loss of foveal functioning although, depending upon exposure conditions, are reversible. Permanent functional changes in achromatic and chromatic acuity can occur in the absence of gross morphological damage and at power densities below the ED_{50} level provided the area of involvement is large. At power densities above the ED_{50} level, little if any permanent and consistent deficits in visual performance are noted if the damage is restricted to relatively isolated areas of either the fovea or parafovea. Multiple pulses which increase the areas of total involvement are more effective in permanently shifting postexposure acuity than is the single pulse condition. The exact nature of the observed loss in visual performance is dependent upon the discrimination task used to assess visual losses.

20. DISTRIBUTION/AVAILABILITY OF ABSTRACT	21. ABSTRACT SECURITY CLASSIFICATION
☐ UNCLASSIFIED/UNLIMITED ☒ SAME AS RPT. ☐ DTIC USERS	Unclassified

22a. NAME OF RESPONSIBLE INDIVIDUAL	22b. TELEPHONE (Include Area Code)	22c. OFFICE SYMBOL
Mary Frances Bostian	301-663-7325	SGRD-RMI-S

DD Form 1473, JUN 86 — Previous editions are obsolete. — SECURITY CLASSIFICATION OF THIS PAGE

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MIDTERM REPORT

30 October 1987 - 29 October 1989

MAY 1990

Supported by

U.S. Army Medical Research and Development Command
Fort Detrick, Frederick, Maryland 21701-5012

CONTRACT NO. DAMD17-88-C-8032

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FOREWORD

In conducting the research described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Research Council (NIH Publication No. 86-23, Revised 1985).

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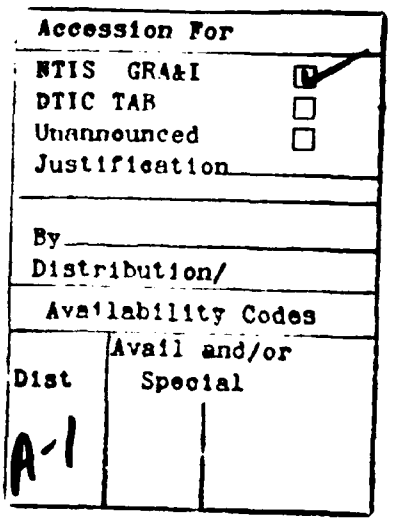

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INTRODUCTION

Technological advances in laser development have produced higher power, more useful devices that are being more frequently employed in a variety of military, industrial, and medical settings. Associated with these developments is the increased threat of ocular damage as the result of intentional or accidental exposure. These newer systems are capable of delivering short pulses of both visible and invisible irradiation which are significantly more powerful than their original counterparts which produced continuous streams of lower energy light.

Any bodily tissue which can absorb the incident light has the potential of being altered as a result of thermal, mechanical, or photochemical damage. A tissue's damage threshold will be dependent upon the amount of energy absorbed, its dissipation over time and the physical characteristics of the tissue itself. Overabsorption can result from a brief, single exposure or from multiple exposures to energy levels which initially might produce no observable consequences. The eye, a delicate organ and photodetector by nature, is especially vulnerable to damage from light absorption. Dependent upon output energy and wavelength, damage can be restricted primarily to the cornea or to the electrochemically active retina. While damage to the cornea can be extremely painful and can alter the transmission properties of the cornea, damage at the retinal level can produce either temporary or permanent blindness.

For the soldier, even temporary visual impairment could jeopardize the individual's ability to complete a visual-motor response and thereby imperil either the soldier or follow soldiers from the successful completion of a mission. Hence, the establishment of safe operating guidelines, development of protective devices against accidental exposure, and the determination of the visual consequences of any type of retinal exposure must remain a high priority in any laser program.

As a first step, the minimal energies necessary to elicit ocular damage must be derived using a variety of acute and chronic exposure conditions. These thresholds can be determined by traditional morphological means (fundoscopic or histologic verification of tissue damage) or can be defined in terms of changes in the visual sensitivity (behavioral or electrophysiological analyses of retinal function). In many ways the latter criteria may be the most important criteria since these standards relate more directly to the ability of an operator to successfully complete a visually-guided response. Furthermore, legal liability for treatment and provisions for disability will ultimately depend upon the demonstrated presence of perceptual dysfunctions.

Advances in other fields such as histology and electrophysiology have greatly improved the analytical methodology for assessing retinal damage from over-stimulation. These procedures have shown that moderate as well as intense light can produce permanent changes in retinal morphology (1, 2, 3). As a result, predicted and observed damage thresholds have become inconsistent, in part due to the differential sensitivities of the various assessment techniques employed. In addition, inconsistencies have resulted from the growing diversities within the delivery systems of newer laser devices.

Histopathological examination (4,5,6, 7) of exposed retinae reveal damage at lower exposure levels than are typically observed by traditional ophthalmological examinations alone especially when the area of retinal involvement is restricted. The photoreceptor outer segment has become the primary damage site (8,9) especially when low energy exposures are employed. The isolation of initial damage at the receptor level is significant since this is also the site of the initial transduction of radiant energy to electrochemical energy, a process that is fundamental to the whole basis for vision. Since the visual receptor cell is a photochemical device, photochemical changes associated with abnormally high levels of light absorption might also lead to damage thresholds not easily depicted by morphological criteria alone regardless of how molecular those measures may be.

Given these facts, the employment of functional criteria might be more relevant in determining safety threshold and might produce lower energy values upon which to base our safety standards. Even with functional criteria, however, thresholds for

permanent shifts in visual sensitivity have varied depending upon the visual task used. Changes in the luminance, wavelength and contrast of test targets have yielded various damage thresholds but most are considerably lower than those derived using traditional morphological criteria. Relatively recent improvements in the behavioral techniques for assessing functional impairment (10) have even further lowered the damage threshold and provided the opportunity for the examination of the transitional zone between temporary and permanent shifts in visual acuity. The elimination of anesthesia for placement of acute laser exposures, which was a part of all previous behavioral studies (9, 11, 12, 13, 14), has allowed for the measurement of transient acuity changes during the initial phases of the recovery process and the exploration of power levels below those that produce permanent shifts in visual functioning. The present report utilizes this methodology for exposing awake, task-oriented animals.

Since the damage mechanism for relatively low energy exposures is likely to be influenced strongly by photochemical alterations (2), the quantal efficiency of the particular wavelength (15) used becomes a critical factor in influencing the severity of the damage. Other factors include the thermal properties of the eye (e.g. diffusivity), retinal position, and the energy density, duration, and spatial extent of the exposing beam. Because there are so many factors involved, no clear boundaries exist for each type of damage mechanism and, in fact, there are thought to be several transitional zones where more than one mechanism may be operating. For instance, it has been suggested that thermally enhanced photochemical effects may occur when tissue temperature rises alone are not adequate to cause thermal injury.

Photochemical alterations in the retinal biochemistry prevent the natural cyclic mechanisms of the photoreceptors to function normally. Several chromophores may be involved. The effects of these alterations may develop more slowly (16, 17) then the more immediately observable consequences of thermal or mechanical injury. To date, there has been no systematic examination of any differential effects these damage mechanisms may have on visual sensitivity.

It has been shown that thermal damage occurs when the radiant energy of incoming photons is absorbed by biomolecules (mainly melanosomes of the retinal pigment epithelium or RPE) and then is converted to heat, resulting in a temperature rise of at least 10^{o} C over ambient temperature in the neural retina, RPE and/or choroid. Such temperature increases prompt the denaturation of proteins with loss of tertiary structure and possible polymerization. Temperature increases of greater than 10^{o} C may cause irreversible denaturation, with permanent loss of tissue function. This thermal mechanism is a rate process (18, 19), a fact shown both empirically (20) and in the many theoretical models of the mechanism that exist (21). Birngruber (22) demonstrated that the degree of temperature rise is a function of various parameters of the exposing light including its energy density, duration, and wavelength, as well as a function of the optical and thermal properties of the biological tissue. Because of the time-energy interdependence, no one threshold can be established, but generally thermal injury cannot occur for exposure durations of less than a microsecond. Models also predict a direct relationship between spot size and temperature rise and equilibrium time which has been confirmed empirically by Cain and Welch (23). Generally, the larger the retinal image of the beam, the lower the power density needed to form a threshold lesion. Thermal lesions are generally homogeneous due to significant thermal diffusion, although they may be smaller than the laser beam size since maximum temperature and therefore maximum damage occurs in the center of the laser beam image.

Mechanical damage occurs in the retina when high power, short duration exposures cause the propagation of sonic waves in the ocular tissue. The pressure front generated within the RPE and/or choroid may cause microexplosions in, for example, receptor cells. Damage may then occur as the result of displaced bulk. Vaporization may accompany the mechanical effects, resulting in the formation and collapse of large cavities, which are often seen as splits in the inner plexiform and nerve layers. Mechanical thresholds are inversely related to time, with thresholds lowest in the picosecond range. Lesions caused by mechanical insult are less

homogeneous than thermal lesions, tending to follow the spatial distribution of the energy in the exposure.

Due to the nature of laser safety investigations, the use of human subjects poses serious methodological and ethical problems that are not easily resolved. As a consequence, intentional human laser exposure has been limited to those eyes that suffer severe retinopathies or eyes which are slated for enucleation. The degradation of such eyes as well as the usual medical urgency for their removal prevents the performance of complete postexposure testing on these subjects (24, 25). Accidental laser exposures in humans are also a means of investigating light effects although in these patients it is often difficult or impossible to reconstruct the exact parameters surrounding the exposure. Furthermore, these patients are often unavailable for systematic follow-up investigations. As a consequence, most behavioral studies have relied on suitable animal model for their investigations.

The selection of the rhesus as our animal model was based on the similarity of its retinal anatomy, physiology, and visual sensitivities compared to that of the human. Some discrepancies do exist in photoreceptor densities (26) and spectral transmission of light (27, 28) although morphologically the rhesus is quite similar to the human. Likewise, some minor differences exist in visual resolutions and spectral sensitivity between the two species although here again the differences are minor (17, 28, 29, 30, 31, 32, 33). The position of this species on the phylogenetic scale and its implied superior intellectual abilities, however, would lead one to assume that the strategies employed by these animals to compensate for any visual function may not be significantly different from those employed by their human counterparts.

The purpose of the current project is an attempt to delineate the immediate and long term effects that single and repetitive Nd/YAG pulses have on gross retinal morphology and visual functioning. In the initial phases of this project, all exposures have been restricted to the 532 nm visible line from a standard Nd/YAG laser. No exposures have been made at the 1064 or 355 nm outputs. Various parameters of the exposure presentation have been varied including position of the laser spot on the retina, site, spot diameter, energy per pulse, and the number of pulses per exposure. Likewise, variations in viewing conditions (wavelength, luminance, and contrast level) have been used in an attempt to assess coherent irradiation influences both the photopic and scotopic systems.

Although much work has been done in this area, there is still much to be accomplished not only to protect human observers from accidental exposure but also to prevent underutilization of lasers because of unrealistic restrictions placed upon its employment. Of particular concern remain the consequences of repetitive exposures over minutes, hours, or days at levels below the ED_{50} for the single exposure condition. In addition, the extent and duration of any deficits elicited need to be further examined under a wider variety of viewing conditions to more accurately estimate performance losses in real-life situations.

METHODS

The method used to expose awake, task-oriented rhesus monkeys has been presented elsewhere (35) and will be only briefly discussed here. This method provides a reliable means of isolating punctate laser exposures onto specific regions of the retina without the use of anesthesia or other means of restraint. The method allows for the assessment of visual performance prior to, during, and immediately following such laser exposures.

Subjects. Male rhesus monkeys ages 2 through 8 years and weighing 8 to 10 lbs were used as experimental subjects. No refractory errors or morphological abnormalities were observed in these animals' retinae and their pre-exposure visual acuities were within normal range for a variety of test conditions.

Subjects were housed individually in standard primate cages and were free to move about in their home environment. Prior to testing animals were fitted with a permanent light-weight, plastic neck collar which was used for capturing and securing the animal in the test apparatus. The home environment was enriched with a variety of activities including TV, radio, food mazes, and play activities during non-testing daylight hours. Light/dark cycles as well as temper-

ature and humidity were controlled. The animals' diets and liquid intake were monitored and the animals were under veterinarian supervision. Each animal was routinely TB tested.

Apparatus. A portable restraint device was developed as a alternative to chronic chairing (35). This apparatus permitted easy removal and transport of animals from their home cage to the experimental chamber without the use of any form of anesthesia or excessive physical force. Restraint was necessary to maintain the animal's correct line of fixation and distance from the viewing screen. Such positioning was an essential part of the methodology for accurate measurements of visual acuity and for pre-determining placement of exposures on the retina. One of the major drawbacks to the use of nonhuman primates is that they can be very difficult and even dangerous to handle. This is especially true as the animal ages and when visual functioning is reduced due to laser exposure. Historically, when an experimental paradigm required even temporary restraint on a daily basis, chronic restraint devices such as primate chairs were employed. Since the experimental paradigm requires an extended time period for completion, this type of restraint was judged to be detrimental to both the welfare of the animal and the purpose of the experiment. On the other hand, daily administration of anesthesia was also judged to be undesirable since it might not only disrupt the experimental procedures, but also would be contraindicated medically.

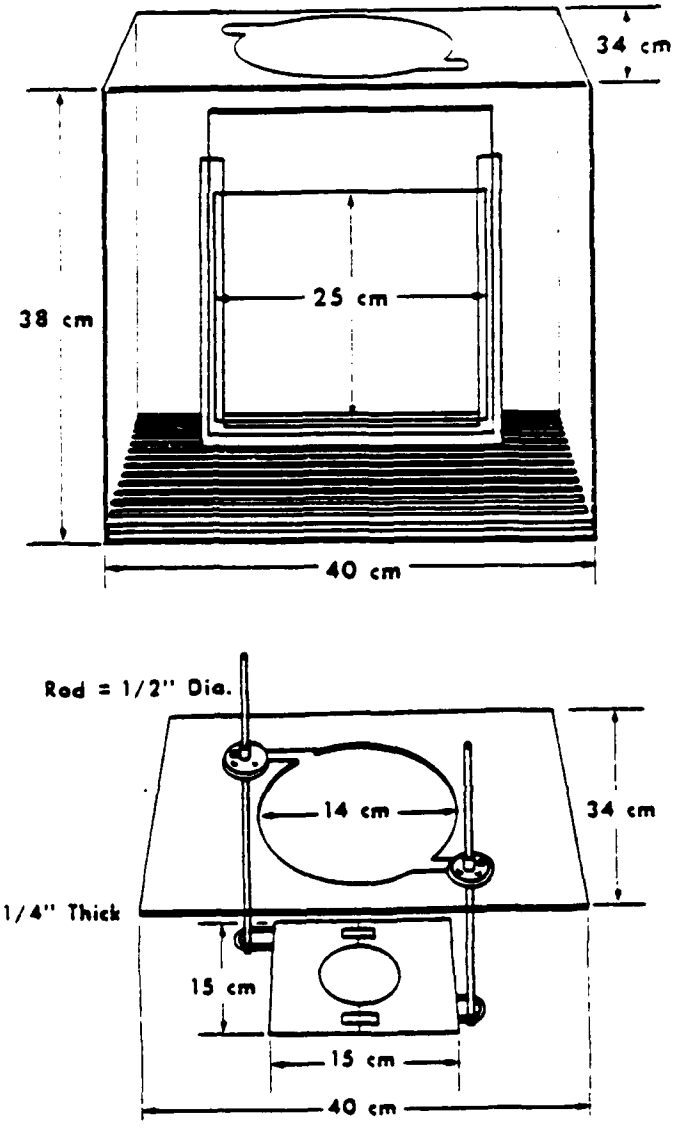

Figure 1. Diagram of the Plexiglas restraint device used during laser exposure and acuity testing. The overall dimensions of the cage as shown can readily accommodate animals of various sizes. A diagram of the collar, worn by the monkey, is shown in the lower diagram. Poles were used to withdrawal the animal's head through the hole in the top of the device and to secure the animal in position.

Our animals have been conditioned to enter a specially designed squeeze device which can be easily converted to a temporary restraint-type chair. The restraint device, which can be mounted on the front of an animal's home cage, is shown in Figure 1. Initially, animals were conditioned to enter the device to receive a food reinforcer. Once inside the device, the animal's head was elevated with poles attached to the light-weight collar that was permanently worn by the animal. The restraint device was then moved into the test chamber and locked in position. Once inside the chamber, the animal was then fitted with a Plexiglas helmet to minimized head movements. An opaque facemask with adjustable iris diaphragms was aligned with the animal's pupils so eye position could be precisely established. Animals were positively reinforced with either fruit or juice for cooperative behavior.

Laser exposures and assessments of visual performance were made in the same light-tight, sound attenuated chamber. Both the experimental chamber and surrounding room housing the image and laser optical systems were painted black to minimize light scatter. A white noise generator was used to

mask sounds generated by the experimental equipment. Mounted on the far wall was a rear projection screen subtending 3 deg at a distance of 1 m from the animal's pupil. Two carousel projectors, positioned outside the chamber, served as the source for image projection and the background of the viewing screen. Luminances and wavelengths of test targets and backgrounds were produced independently by neutral density and interference filters placed in the light paths. Both projectors were programmable and were internally able to optically read a variety of coded slides.

Acuity was measured using standard Landolt rings and gapless rings which were photographically produced on Kodak high contrast film (Kodalith). The rings were black on a clear background. The thickness of the Landolt rings and the width of the gap that formed the critical detail were always 1/5 of the diameter of the ring. The size of the gap could be varied from 0.25 to 30 min of visual angle in equal steps. The position and orientation of the gap in the Landolt rings was invariant. Except for the screen, the test chamber was entirely dark.

The presentation of slides, recording of the animal's responses, and reinforcements were under computer control. A Cyborg ISAAC interface and Labsoft logic was used for programming purposes. All data was stored and analyzed on a standard IBM PC.

Discrimination Task. Animals were trained using an avoidance paradigm to press a lever in the presence of a Landolt "C" and not to respond in the presence of gapless rings of equal dimensions. Failure of the animal to press the lever in the presence of a Landolt "C" (defined as "miss") or lever pressing in the presence of gapless rings (defined as a "false positive") resulted in the presentation of a discriminative tone and, on a variable reinforcement schedule, a brief, weak electrical shock. The negative reinforcer, produced by a high-tension coil, was annoying but not highly painful as the author can testify from experience. Swinnen, Brady & Powell (36) concluded that because of its short duration this type of shock is safer than conventional electric shock. Our animals demonstrated no reluctance to enter either the restraint cage or experimental chamber also indicating that the shock had no lasting psychological importance. The use of negative reinforcement was necessary in order to consistently maintain the animal's vigilance during the course of testing and immediately following laser exposure. A vigilant animal could avoid shock altogether.

Threshold acuity was derived using a modification of the von Bekesy tracking technique (37). In this technique, if the subject correctly detected the Landolt ring by pressing a lever (hit), a discriminable tone was presented and the next presented series of Landolt rings and gapless rings was 10-20% smaller. Incorrect detection of the Landolt ring (miss) resulted in a different discriminable tone, the possibility of a brief shock on either a fixed or variable ratio schedule, and the presentation of rings 10-20% larger. To discourage the animal from responding indiscriminately to all rings, a third discriminable tone was presented immediately following lever responses to gapless rings (false positive) and, on a fixed ratio schedule, the animal received a brief shock for these incorrect responses. The number of false positive responses was always low in trained animals (less than 10%). Using this paradigm, the size of the target was always at the animal's threshold thereby eliminating time which would have been spent testing targets either significantly above or below threshold. The test objects were typically presented in sets of four rings that were of equal diameter. Three of the rings in each set were gapless, while the fourth was a Landolt "C" that appeared in a random position within the set. Each ring was projected for 2 sec. and there was a 1 sec. dark interval between successive rings. The size of the test series was shifted only on responses to Landolt "C" rings and not to gapless rings. Baseline means, variability, and false positive responses in both the exposed and control eye were determined daily throughout the experiment. All measurements were made under monocular conditions and after the animal had adapted to the luminance level of the screen.

Laser System. A Nd\YAG laser(Molectron MY 32-20) served as the primary exposure source. Only the 532 nm line was used in this study, the invisible lines were blocked internally. The power densities of the beam were controlled by adjustments at the laser head and by neutral density filters placed in the beam pathway. Power densities were measured with a volume

absorbing calorimeter (Scientech, Model 363) and were expressed in uJ at the cornea. A small HeNe laser was used for aligning purposes. A diagram of the optical system is shown in Figure 2. The laser optical system produced a collimated beam of adjustable diameter from less than 50 microns to greater than 1,000 microns on the retina. Proper alignment of the laser beam with the animal's pupil and retina was critical. To align the beam, it was presented coaxial with a line between the artificial pupil and the gap in a specified threshold Landolt ring which subtended less than 1 minute of arc. For determinations of the line of sight, a 2 mm aperture was placed on the screen over the position of the gap in the specified Landolt ring. A mirror, approximately 2 m behind the 4 mm artificial pupil was then adjusted until it was normal to the line of sight. With the converging lens removed, the beam splitter at the junction of the image and laser beams was then aligned so that the collimated beam from the laser past through the 4 mm aperture and was reflected off the mirror back onto itself and through the 2 mm aperture at the projection screen. Coaxial alignments with the line-of-sight were then verified by noting that the reflected beam passed through both apertures and back on itself without any loss. The focusing lens was then positioned such that the cornea was in the focal plane of the lens and so as not to change the alignment of the beam with the line-of-adjustment. Presenting the beam in Maxwellian view reduced the possibility that changes in pupil diameter or small lateral movements of the animal's head would affect

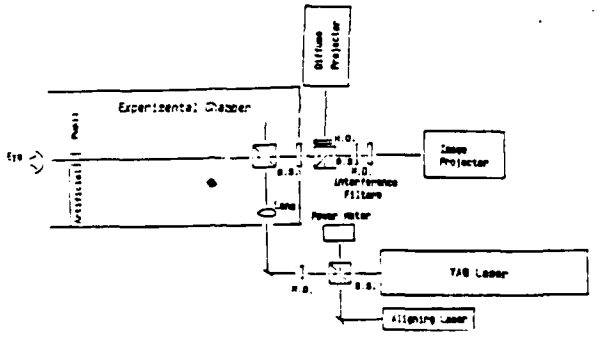

Figure 2. Diagram of the laser and image optical system. The laser beam was presented using a Maxwellian view and coaxial to the gap in a threshold Landolt ring. An CW Argon laser, not shown, could also be used for laser exposures and was positioned parallel to the Nd/YAG laser.

the amount of light entering the eye. The location of the exposure on the retina (on- or off-axis) could be varied by adjusting the position of the beam relative to the animal's point of fixation on the viewing screen.

Laser exposure. Prior to any laser exposure, stable acuity levels were established for each eye under a variety of different chromatic, luminance, and contrast conditions. Fifteen minutes prior to each exposure, acuity was again derived and failure of the animal to obtain a mean acuity within one standard deviation of his predetermined acuity level aborted the laser exposure. Session variability or an increased false positive response rate beyond a pre-established level also aborted the exposure session. In cases where the animal did not achieve his pre-exposure baseline level in an eye which had previously been exposed, testing was continued to establish the parameters of the visual deficit.

The laser flash was triggered immediately after the animal correctly detected a specified threshold Landolt. No exposures were made following incorrect detections of threshold targets or following correct detections during the final 1 sec of the trial. Using this procedure for large diameter spots immediate and significant downward shifts in acuity were noted in over 90% of the exposures presented. In those cases where no such downward shifts in acuity were noted, it is possible that involuntary or pre-established voluntary eye movements may have lead to exposures in the peripheral regions of the retina. Given the nature of our acuity task, exposure of these regions of the retina would have been difficult or impossible to detect. Control or sham exposures with the laser beam blocked at the point of the safety shutter tested for any factors within the procedure which might change the animal's expectancy or response criterion.

Only one exposure session was scheduled per day and in cases where the animal failed to return to his pre-exposure level during the immediate postexposure session, no exposures were made on subsequent days until a new baseline acuity level was established. At each power density, a repeated, random design was employed for each of the different types of viewing conditions employed. The order of laser power densities presented was fixed, beginning first

with the lowest and increasing in a stepwise order following completion of all viewing conditions. Postexposure testing was terminated after the animal had regained his pre-exposure acuity level for the given viewing condition or after 90 minutes of testing whichever came first. The animal's unexposed eye served as a control.

Statistical analyses of the data. Statistical comparisons were made of the changes in the degree and duration of the initial deficit as well as the total time for full recovery for the different exposure energies, durations, and spot sizes employed. Also examined was the effect that the nature of the acuity task had on the magnitude and duration of the visual deficits.

The determination of the animal's performance level using the tracking technique was derived using the formula developed for the "Up and Down" procedure (38). Normally an animal's acuity was averaged for each running two minutes of testing before and after exposure.

RESULTS

Sample data demonstrating the effectiveness of our procedure to place

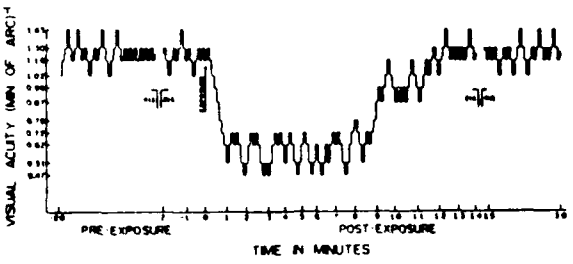

Figure 3. Sample raw data demonstrating the immediate drop in visual acuity immediately following laser irradiation. The occurrence of the 100 msec, 7mW, 632.8 nm exposure is indicated in the figure by an arrow, and corresponds to the zero point on the abscissa. The ordinate indicates the various sizes of the gaps in presented Landolt rings and is plotted in reciprocal visual minutes of arc. This scale is measured in discrete steps, since the vertical excursions of the plot were taken from a non linear potentiometer mounted on the slide tray of a carousel which recorded tray position. The abscissa represents the presentation of the Landolt C's; corresponding times (in minutes) for representative trials are indicated relative to exposure.

foveal exposures in an awake, task-oriented animal is shown in Figure 3. In this example the animal was exposed to a single 100 msec flash of 632.8 nm coherent light presented coaxial with the gap in a threshold Landolt ring. Time, relative to exposure, is indicated on the abscissa. A pre-exposure mean acuity of 1.25 $(\text{min of arc})^{-1}$ was measured during the first 15 minutes of testing using a 4:1 ratio of gapless rings to Landolt C's (left portion of figure). Immediately preceding the exposure, the S was transferred to a 2:1 ratio of gapless rings to Landolt C's and tested for an additional 2 min. This ratio shift was typically used to more rapidly access acuity shifts and did not affect either the animal's response criteria or false positive rate. In this example, immediately after exposure, the animal's acuity decreased to 0.51 $(\text{min of arc})^{-1}$, which corresponds to an acuity deficit of 59% relative to its pre-exposure acuity. This visual deficit lasted 9 min before the subject's acuity gradually returned to its mean pre-exposure level. Total recovery from the initial deficit was complete in approximately 13 min. Threshold testing using the 2:1 ratio of gapless rings to Landolt C's was continued for 3 additional minutes. The ratio of gapless rings to Landolt C's was then shifted back to 4:1, and postexposure acuity measurements were extended for an additional 15 min. No permanent shift in pre- and postexposure acuity was found at the energy level (7 mW) used in this figure.

When more intense laser exposures were presented over a significantly shorter duration and involved a more restrictive retinal region, the consequences of the exposure on visual functioning were not necessarily more prolonged or greater in magnitude. Figure 4 shows the immediate changes in an animal's visual acuity following a foveal exposure to a single, 15 nsec pulse of 532 nm coherent light. The energy of this pulse, 50 uJ, was significantly above the ED_{50} for this exposure condition and likely produced a small, ophthalmologically visible lesion. Due to the small laser retinal image (<50 microns) and the brief duration (15 nsec) of the exposure, the size of lesion would be extremely small and should therefore only partially disable this animal's foveal capabilities. Immediately after exposure, the animal's visual acuity decreased by approximately 70% (to a Snellen acuity of 20/75) and then acuity gradually recovered over the next 20 minutes

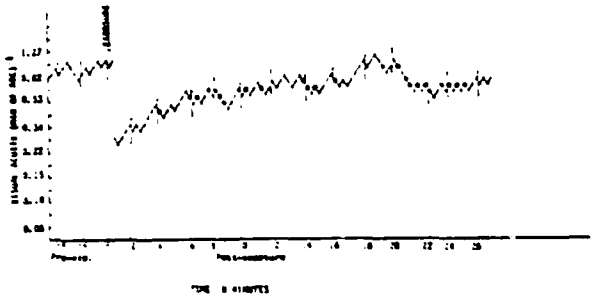

Figure 4. Threshold acuity following a single, 50 uJ pulse. The vertical lines through the data represent two minute time marks. Beam diameter on the retina represented less than 50 microns and was presented coaxial with a point on a visual target where the animal was required to maintain fixation.

to its pre-exposure level before again decreasing from this baseline by 25% to an acuity level of 20/30. The animal remained at this slightly depressed level for the remaining 10 minutes of the test session.

Although this animal showed a lesser deficit in terms of its initial effects and appeared to recover during the exposure session, neither this animal or others similarly exposed appeared to be able to maintain their previously consistent visual performance. Typically prior to exposure an animal's pre-exposure acuity was remarkably consistent varying little either within or between daily test session. Following exposure, however, these animals' between session variability greatly increased in the

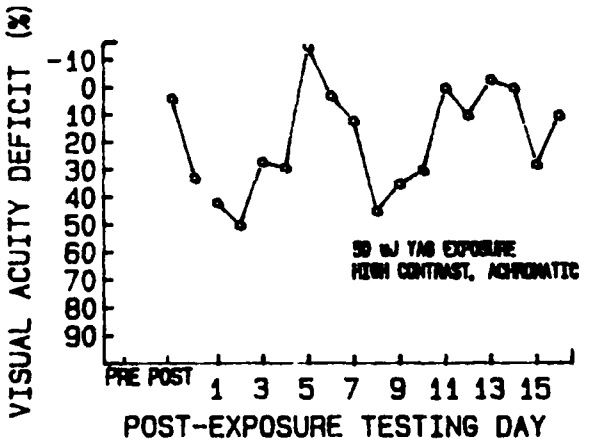

Figure 5. Daily mean postexposure acuity. This subject was exposed to several 50 uJ, 532 nm pulses separated in time by several days. Each data point represents the average deficit over a 30-45 minute test session where no laser exposures were made.

exposed eye from that observed prior to exposure. An example of this inability to maintain a consistent baseline visual acuity in subsequent testing sessions is shown in Figure 5 for the same animal as shown in Figure 4. As this figure demonstrates, the animal's average daily acuity following exposure could be depressed as much as 50% from its pre-established baseline level. No significant trends were observed over the postexposure testing period of several weeks and within session variability was not as markedly affected. These animals became increasingly reluctant to be tested. No significant shifts were noted in their control or unexposed eye.

The effects of multiple exposures presented over a period of several weeks is shown in Figure 6. This exposure produced a minimum diameter (<50 microns) spot and was presented coaxial with the animal's fixation point. This animal was repeatedly exposed to single, 15 nsec pulses from a Nd/YAG laser (532 nm) at an energy of 50 uJ per pulse. No more than one exposure (pulse) was given per day. The energy density of this pulse was above the ED_{50} for this exposure condition although given the size and duration of the exposure, the retinal area affected would be minimal. Immediately after the first exposure, the animal's visual acuity was decreased significantly but the deficit was rather short lasting. Within 10 minutes, the effects of this exposure had completely disappeared and the animal's visual performance was again within normal limits. No significant long term effects were noted and, after re-establishing the animal's pre-exposure baseline in a subsequent test session, the animal was again exposed to a second, then third and fourth 15 nsec pulse. Each time the magnitude of the initial deficit was approximately the same but the total time for full recovery progressively increased. By the fourth exposure, full recovery was not complete within the immediate 30 minute postexposure test session and the animal's average postexposure performances in subsequent sessions demonstrated the type of variable performances shown in Figure 5.

In order to further delineate the nature of any elicited performance changes in those animals who had previously been repeatedly exposed to intense, but highly spatially restrictive, Nd/YAG pulses, postexposure visual performance was

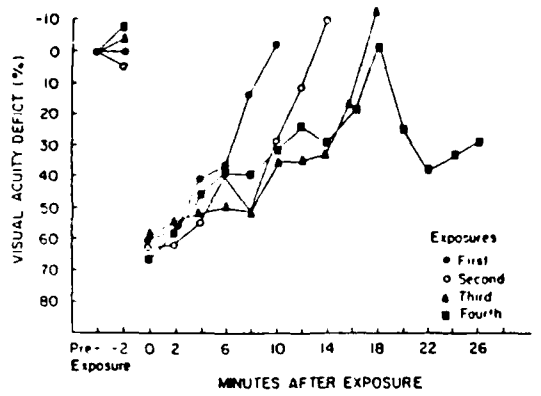

Figure 6. Effects of multiple, 15 nsec pulses on visual performance. The energy density per pulse was 50 uJ and the diameter of the spot on the retina was less than 50 microns. Acuity was measured using high-contrast, achromatic targets.

measured using different contrast targets placed on backgrounds of various wavelengths. Figure 7 demonstrates the shift in acuity over a 4 week postexposure period to targets of varying contrast. Previously, this animal had received a series of 15 nsec, 50 uJ Nd/YAG pulses. The animal's pre-exposure acuities were maximum when intermediate contrast (80%) target were employed. Two weeks following the last exposure, this animal demonstrated no differential sensitivity to targets varying in contrast between 60% and 98%. For all contrast targets, acuity was significantly depressed (representing a Snellen acuity of 20/50)

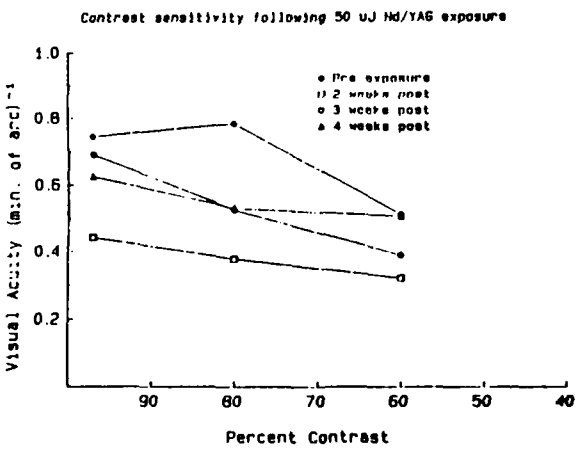

Figure 7. Postexposure acuity to various contrast targets. This animal was exposed to a series of 50 uJ, 15 nsec pulses from a Nd/YAG (532 nm) laser. Postexposure acuity for each contrast target was measured over a period of four weeks. The data presented here represents the average acuity over a 10-15 test session for each of three different contrast targets (60%,80%,98%).

although the depression was slightly more for the lowest contrast targets. Within 4 weeks of exposure, the animal's visual performance had increased significantly for all contrast targets and the animal demonstrated the greatest sensitivity to the highest contrast target and the least to intermediate contrast targets.

This same animal's postexposure acuity was measured using darkened rings on chromatic backgrounds. The various wavelength backgrounds were equated for equal numbers of quanta. Since the animal's task was to depict the presence of a minimal gap (lighted area) within the darkened ring, this task can be considered an indirect measure of the animal's sensitivity to various

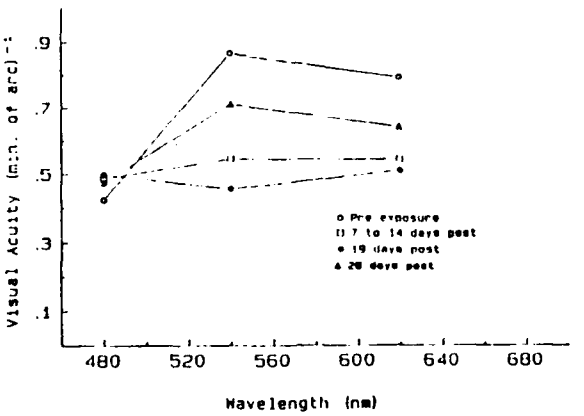

Figure 8. Spectral acuity in one animal following repetitive 15 nsec pulses of 50 uJ Nd/YAG light. This animal was exposed to only one pulse per day and the four exposures of minimal spot diameter (<50 microns) were given over a period of several weeks. Darkened rings were presented against different chromatic backgrounds which were equated for equal numbers of quanta. Each data point represents the mean acuity of a minimum of twenty minutes of threshold acuity measurements.

wavelengths. In this figure only three spectral backgrounds were chosen. In pre-exposure testing the animal demonstrated maximum visual acuity when the darkened figure was against a 540 nm background although the animal also maintained a heighten acuity to targets against a 620 nm background. Significantly poor visual performance was noted when the background was shifted to the short wavelength region (480 nm) of the visual spectrum. Following exposure the entire function was depressed and remained so for several weeks before the animal partially

recovered sensitivity to intermediate and long wavelength backgrounds. Sensitivity to short wavelength backgrounds remained unaltered.

In the previous figures the effects of repetitive pulses at or above the ED_{50} were shown. This paradigm was used to delineate any cumulative effects that might occur. The initial effects of a single 10 uJ pulse are shown in Figure 9. This figure represents the raw data as derived from our up-down threshold procedure. The size of the threshold Landolt rings are indicated on the y-axis and are represented in this figure

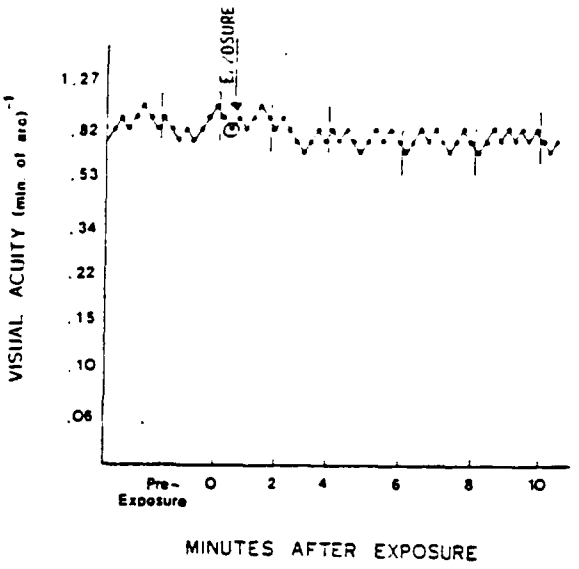

Figure 9. Sample data of threshold acuity prior to and immediately following a single 15 nsec, 10 uJ pulse of 532 nm coherent light. Beam diameter on the retina represented less than 50 microns and the spot was presented coaxial with the gap in a threshold Landolt ring. The vertical lines through the data represent 2 minute time marks. Each filled circle represents the presentation of Landolt ring and the vertical lines between circles represent the presentation of gapless rings of the same diameter.

by filled circles. The time of exposure is shown by an arrow and indicated as the zero point on the time axis. The 15 nsec exposure was presented coaxial with the gap in a threshold Landolt ring. No immediate impact of this exposure on baseline visual performance was noted even though the energy of this pulse was slightly above the ED_{50}. There was, however, a gradual downward shift in baseline acuity with prolonged postexposure testing although the effect was extremely weak and statistically insignificant. Daily exposure of this animal to 10 uJ pulses, however, did increase the magnitude of the immediate acuity deficit but did not produce a permanent shift in baseline visual acuity when achromatic targets were used to access visual sensitivity.

In some cases, the presentation of a single Nd/YAG pulse did produce a shift in visual acuity although the deficit was again somewhat reduced and much shorter in duration than that observed when using exposures of lesser energy but presented for longer time periods. Figure 10 demonstrates the percentage loss in visual acuity immediately following a minimal diameter, 2 uJ, Nd/YAG pulse. This figure demonstrates that the animal experienced an immediate 25% loss in visual acuity within 3 minutes of exposure followed by a full recovery within seven minutes of exposure.

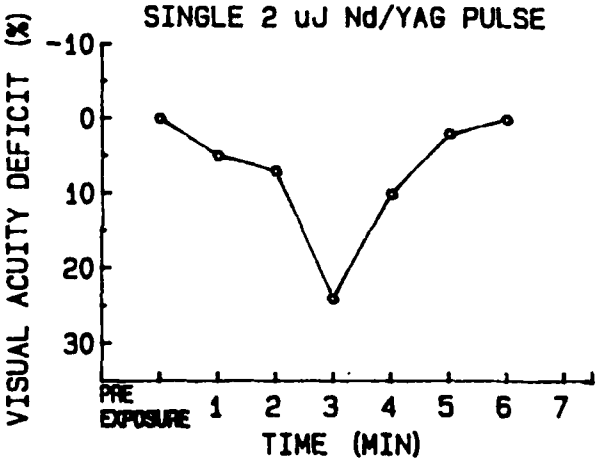

Figure 10. Percent loss in visual acuity following a single 15 nsec, 532 nm pulse from a Nd/YAG laser. The minimal diameter spot was presented on axis and the average acuity for each two running minutes prior to and immediately following exposure is represented in relation to the animal's pre-exposure baseline (visual acuity deficit).

Since the impact of any laser exposure is a function size of the area involved as well as the energy of the pulse, we have explored the impact that changes in retinal spot size have on the magnitude and duration of the elicited deficit. Using a 15 nsec pulse virtually eliminated any impact that either voluntary or involuntary eye movements might have on the size of the retina irradiation. The impact that varying spot sizes from 200 to 500 microns on the retina has on the magnitude of the initial deficit is shown for one animal in figure 11. For

relatively small diameter exposures the magnitude of the initial deficit was approximately 15% while for relatively large diameter exposures this deficit increased to approximately 30%. Between these two extremes, an almost monotonic function was noted for this effect.

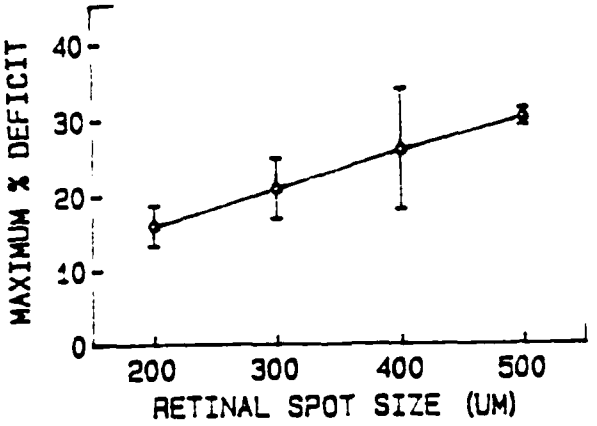

Figure 11. Effects of spot size on the magnitude of the initial deficit. This subject was exposed daily to a single, 3 uJ pulse from a Nd/YAG laser. The exposure was presented on-axis. Acuity was measured using a high contrast, achromatic target. Each data point represents the mean deficit of several different exposure sessions and the vertical bars represents ± 1 SD.

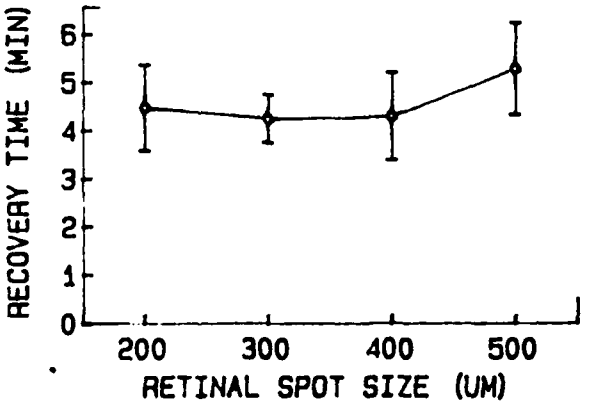

Figure 12. Effects of spot size on recovery time. This subject was exposed daily to a single, 3 uJ pulse from a Nd/YAG laser. The exposure was presented on-axis. Acuity was measured using a high contrast, achromatic target. Each data point represents the mean time for the animal to regain his pre-exposure acuity and the vertical bars represents ± 1 SD over several different exposures for each size image.

For the same animal and exposure conditions, the total recovery was plotted as a function of the different spot sizes. As this figure shows (see Figure 12) spot size did not significantly affect the total time for full recovery and with the specific power density employed, recovery was typically complete within 5-6 minutes following exposure. As seen in previous studies, spot size has its primary effect on the magnitude of the elicited deficit and not on the duration of the deficit. How long it takes an animal to recover from an exposure is primarily a function of the energy density of the flash rather than its image size.

In previous figures we have demonstrated the cumulative effects that multiple exposures separated in time by as long as several days or even weeks have on the magnitude and duration of the elicited deficit in visual performance. Figure 13 demonstrates the adverse effects that a series of pulses presented within a 100 msec window of each other have on visual acuity. In this figure the total energy per exposure for a single session was fixed at 3 uJ. The solid line represents the average recovery

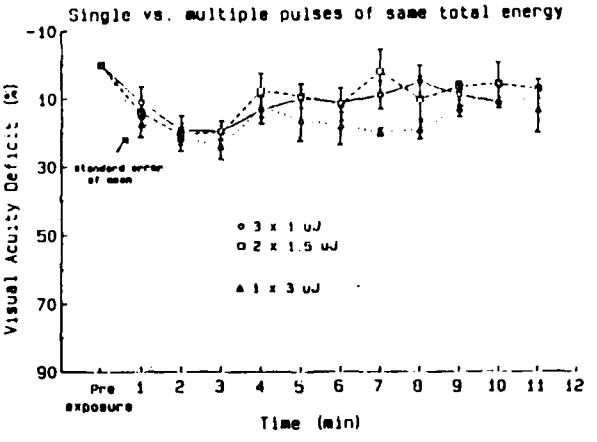

Figure 13. Effects of single versus multiple pulses within the same test session. Total energy per exposure was fixed at 3 uJ and the size of the spot on the fovea was less than 50 microns. In the cases of multiple pulses, all pulses were presented within a 100 msec window of each other to eliminate any effects of voluntary eye movements. A average of five different exposures were made for each condition shown. The vertical bars about each data point represents the standard error for the repeated exposure sessions.

function following three, 1 uJ pulses. In this condition, like in all others, the animal's baseline acuity was minimally affected by the laser exposure. A deficit of only 20% was elicited for the single, double, and triple pulse condition. These deficits lasted several

minutes before partially recovering and stabilizing within approximately 5 to 7 minutes of exposure. Although following some exposures the animal had difficulty maintaining his pre-exposure acuity, in no case were these effects observed 24 hours following the exposure.

In the next two figures a comparison was made of the mean time for total recovery (Figure 14) and magnitude of the maximum deficit (Figure 15) for two animals exposed in a manner similar to that shown in Figure 13. These animals were exposed to 3 uJ from a Nd/YAG laser which was presented either as a single pulse, two pulses, or a series of 3 pulses all presented within a 100 msec window of each other. No more than 3

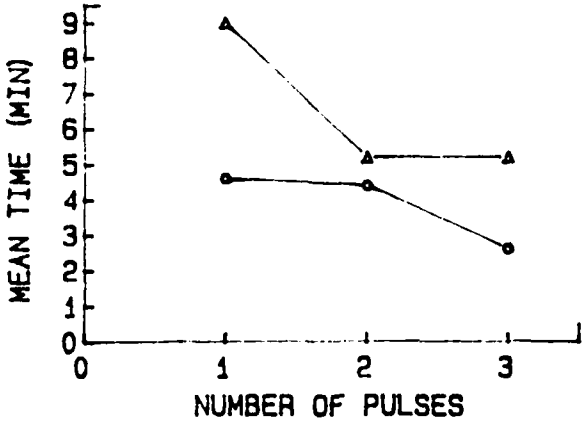

Figure 14. The effect that single versus multiple pulses of same total energy has on the time for full recovery. The data represent mean recovery time for each animal. Each data point represents the mean of 5-7 exposures presented over a series of several weeks. These animals were exposed to either one, two, or three pulses which totaled 3 uJ and represented a on-axis spot size of less than 50 microns. Acuity was measured using high contrast, achromatic targets.

uJ of light were presented per exposure session but these animals received repeated exposures over a series of several months. Figure 14 shows the mean time for recovery from a single versus series of pulses which were equated for total energy. These two curves represent the average data from two different subjects. For one animal the mean recovery time for a single 3 uJ pulse appeared longer (9 minutes) than for either two 1.5 uJ pulses or three 1.0 uJ pulses. For the second animal no observable differences were noted. A statistical test (t-test) of these differences within subjects revealed no significance in either animal and it would appear that three pulses presented within a 100 msec of each other are as effective as a single 15 nsec pulse of equal total energy.

Figure 15 demonstrates the size of the maximum deficit for this same exposure condition. Here again there were no significant differences either between or within animals for the single versus multiple pulse condition.

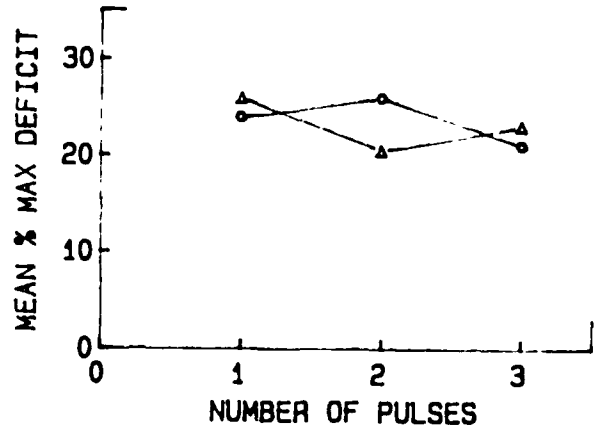

Figure 15. The effect that single versus multiple pulses of same total energy has on the size of the maximum deficit in visual acuity. The exposure conditions in this figure are identical to that shown in Figure 14 for total recovery time. Each data point represents the mean of 5-7 exposures presented over a series of several weeks. These animals were exposed to either one, two, or three pulses which totaled 3 uJ and represented a on-axis spot size of less than 50 microns. Acuity was measured using high contrast, achromatic targets.

Separate from the acute exposure paradigm (single or multiple 15 nsec) this study has also explored the effects that exposure to a prolonged train of relatively low energy pulses (glare) might have on visual performance. In this portion of the project we attempted to simulate the type of performance decrements that might be experienced by someone who must work with or around a low level laser source that might be irradiating a portion of the person's visual field. These exposures have varied in power density, duration, spot size, and position on the retina (on-axis or foveal and off-axis or parafoveal). Position on the retina was established by locating the beam either coaxial with the gap in a threshold Landolt ring or positioning the beam away from the gap. Chronic exposures were produced by a

series of pulse trains from a Nd/YAG laser. Exposure duration was timed through a conventional electronic shutter. Figure 16 demonstrates the effects that relatively brief pulse trains (5, 10, and 60 seconds) have on the magnitude and duration of the elicited deficit. As the figure demonstrates, for all

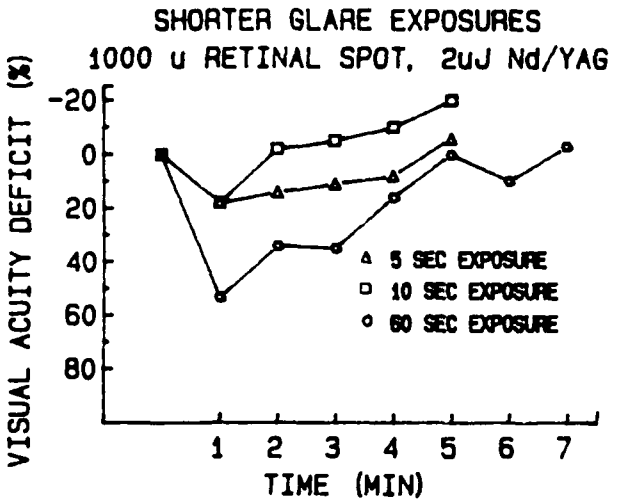

Figure 16. Postexposure acuity following brief exposures to a train of Nd/YAG pulses. The duration of the pulse train varied from 5 seconds to 60 seconds. Only one exposure was made per day and the energy of each pulse was 2 uJ. The beam created a 11000 micron spot on the retina.

three exposures durations full recovery was complete within 7 minutes of its termination. Recovery time was longest and the magnitude of the deficit greatest for the longest duration exposure (60 second) although the differences, especially in total recovery time were not significantly different. For this type of exposure paradigm, it was difficult to accurately assess visual functioning during the actual laser exposure because of its short duration and the limitation of only one exposure per day.

Exposure to relatively prolonged laser light presented coaxial with the gap in a threshold Landolt rings (on-axis) seriously disrupted visual performance during the irradiation regardless of either the energy density of the pulses or its image size on the retina. Figure 17 shows the effects of a 20 minute exposure to low level Nd/YAG laser light. The train of pulses were presented on-axis and varied in spot size from 500 to 700 microns in diameter. As shown, immediately after the onset of the exposure acuity decreased significantly to greater than 90% of its pre-exposure level and the animal had great difficulty in detecting even the largest of Landolt rings while being exposed. Under this condition, this animal did not significantly change his response strategies as seen by a fairly uniform and low false alarm rate, rather his correct detection rate (hit) decreased dramatically and remained consistently depressed for the full duration of the exposure. Once the exposure was terminated, the animal somewhat rapidly regained his pre-exposure acuity level. Full recovery occurred within in approximately twelve minutes. Changes in the diameter of the spot on the retina had little impact either on the size of the maximum deficit or the total time for full recovery. Given the relatively large spot sizes used as well as its position superimposed on the discriminanda, this inability to detect the critical features of targets is understandable.

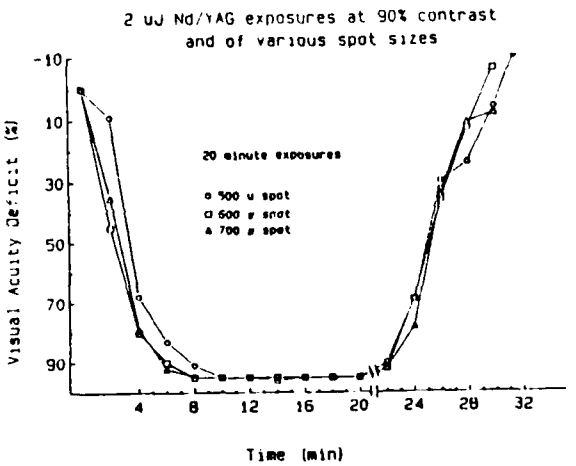

Figure 17. Visual performance changes during and immediately following prolonged exposure (glare) to 532 nm coherent light of varying spot sizes. A 20 minute series of laser pulse trains were presented coaxial with the gap in threshold Landolt rings. The energy per pulse was set at 2 uJ and beam was positioned such that it covered the discriminanda within a visual target and should have prevented the animal from "looking" around the exposed site. The size of the spot on the retina was varied from 500 to 700 microns in diameter.

These same exposure conditions were again tested using a 500 micron spot (on-axis) but with varying energy densities ranging from 1 nJ to 10 uJ. While the animal's visual performance significantly declined in all cases, the magnitude of the deficit was greatest when the highest power density was employed and least when the

energy densities were also the lowest. Total recovery time following the termination of the exposure did not vary significantly with the different power densities employed.

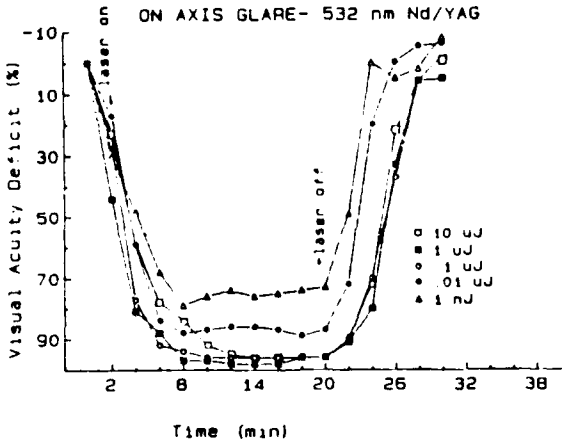

Figure 18. Visual performance changes during and immediately following prolonged exposure (glare) to 532 nm coherent light of varying energy densities. A 20 minute series of laser pulse trains were presented coaxial with the gap in threshold Landolt rings. The energy per pulse was varied from 1 nJ to 10 uJ and the spot diameter on the retina was set at 500 microns. The exposure was positioned such that it completely covered the critical features of the discriminanda within a visual target. The conditions were such that the animal was also unable to "look around" the irradiation and make the required discrimination.

Positioning the laser beam slightly off-axis so that the irradiation did not cover the critical feature of the discriminanda improved visual performance greatly during the actual exposure but also produced some transient and long term deficits in visual performance following its termination. In Figure 19 exposure of the parafoveal retina to 0.5, 1, or 2 uJ of 532 coherent light produced deficits ranging from 30 to 80 percent of pre-exposure acuity. In this experiment the animal was exposed to a train of pulses of one energy density for a given period of time and then the energy density was increased. In the top curve, the animal was first exposed to 0.5 uJ pulses for approximately 8 minutes before the energy density of the pulses were increased to 1 uJ. Four minutes later the irradiation was terminated. In the lower curve the energy of the exposure began at 1.0 uJ and was increased to 2 uJ approximately twelve minutes following its onset. In both cases when the laser light was terminated, visual acuity quickly returned to its pre-exposure baseline. When the energy of the pulses were increased, the animal's acuity decreased and remained depressed until the exposure was terminated.

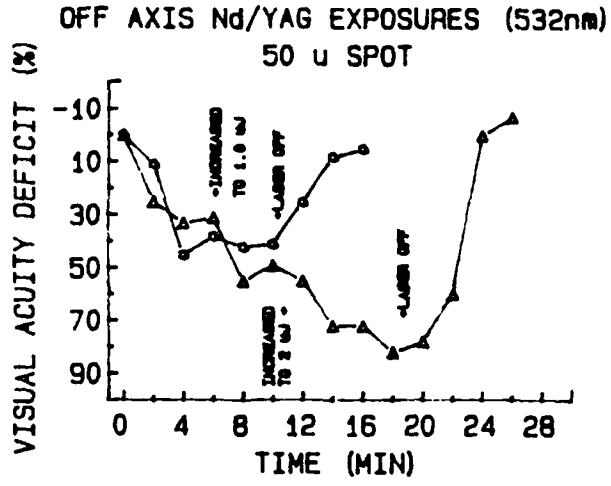

Figure 19. Changes in visual performance during and immediately following prolonged exposure to a series of pulse trains from a Nd/YAG laser. The power density of the exposure varied from .05 uJ to 2 uJ and the beam was position slightly off-axis.

As previously noted the nature of the visual task affects any observed changes in visual performance during and immediately following laser exposure. Using different energy densities and exposure positions (on- and off axis) we have explored what effects target contrast and background wavelengths have on the ability of the animal to correctly detect Landolt rings. A series of representative curves for high (90%) and intermediate (60%) contrast targets are shown in Figure 20. In this example a much less intense, but prolonged exposure was superimposed onto the position of the threshold gaps within the animal's visual field (on-axis). The exposure lasted 46 minutes during which time the animal's visual acuity was continually measured. The impact of this exposure on detection of high contrast targets was less than that observed when low contrast targets were employed. For the high contrast condition, acuity dropped approximately 30% and the animal was able to maintain this reduced visual functioning for the duration of the exposure. Immediately following exposure, only a gradual recovery was noted within the remaining 10 minutes of the test session. Postexposure recovery was complete the

following day. For high contrast targets, on the other hand, the immediate effects of the exposure were more pronounced (a deficit of 70% as opposed to 40%) and the animal appeared to have difficulty in maintaining this performance level as the exposure continued. Immediately following the termination of the exposure, however, the animal more quickly regained some of his depressed visual functioning and again no permanent shift in visual acuity was noted in subsequent test sessions.

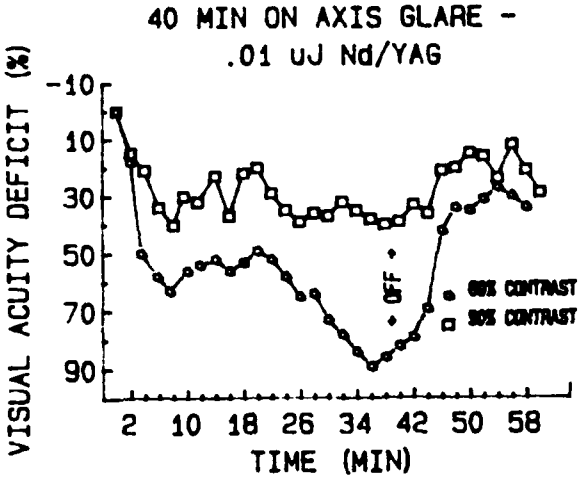

Figure 20. Effects of target contrast on visual performance during and immediately following prolonged exposure to Nd\YAG light. The laser irradiation was presented on-axis at a power density of 0.01 uJ. The exposure duration was 40 minutes.

DISCUSSION

This project at its onset advanced the following hypotheses:

(1). Light induced damage to the retina not only disrupts retinal physiology but also visual functioning. Damage to areas inside the fovea should have more severe effects on visual resolution and color vision while exposure to the peripheral retina may disrupt scotopic vision but should have a lesser effect on fine visual acuity. Clearly, our initial results support this notion although off-axis exposures have been shown to have a greater disruptive effect on foveal functioning than might have been expected although this effect appears more temporary in nature than that which is noted for similar foveal exposures. This effect most likely has little physiological significance but nevertheless could dramatically alter visual performance by initially creating a distraction and then prolonged disruptive afterimage in the exposed area.

(2). The number of foveal photoreceptors altered should affect the magnitude of any visual deficit elicited. A single punctate lesion involving only a limited number of photoreceptors should have little consequence on overall visual acuity but more numerous lesions created by multiple exposures should eventually summate to adversely affect any discrimination requiring fine resolution. Our repetitive exposure data demonstrates that with each successive exposure it becomes increasingly difficult for an animal to "look" around affected regions and still maintain a consistent and elevated performance level. Eventually, these small punctate lesions produce a behavioral deficit similar to that observed when a large area was irradiated and altered during a single 100 msec exposure.

(3). Isolated punctate lesions of the fovea would be expected to increase discrimination errors as critical features of briefly presented targets fall on damaged regions. Our results to date demonstrate an increase in within and between session variability following exposures that "damage" only limited areas (<50 microns) of the fovea. Associated with this increased variability in baseline sensitivity is a change in the animal's false positive rate as well as increases in the time it takes the animal to respond.

(4). Edema within and surrounding the exposed tissue should alter photoreceptor orientation, spacing, and functioning and thereby temporarily create larger disruptions in visual performance than would otherwise be expected. Our results demonstrates that often within several minutes of an intense, punctate exposure a temporary recovery in visual performance occurs followed by a significant deficit either in the same or subsequent test sessions. This deficit was often greatest the day after exposure and some partial recovery was noted over the next several days or weeks of postexposure testing.

(5). Hemorrhages within the retina should also result in a clouding of the ocular media thereby increasing light scatter, creating a blurred image and reducing the fine resolution capabilities of the fovea.

Thus far, our investigations have been restricted to the behavioral analyses of light-induced changes and our exposure energy densities have been at lower levels where serious hemorrhages might not be expected.

(6). Independent of any transient or permanent morphological change, visual acuity could be disrupted by a dazzle effect from less intense laser exposure. These effects should be immediate but transient. As previously mentioned this "dazzle" effect can occur for low-level foveal exposures or for intense off-axis exposures which leave the foveal functioning theoretically unaltered. These effects have been shown to quickly dissipate once the exposure is terminated.

(7). The nature of the observed loss in visual sensitivity should be dependent upon the discrimination task used. Changes in the contrast of the target or the wavelength of the background elicit differential effects. Chromatic targets appear more sensitive in depicting changes in postexposure visual functioning than do achromatic targets as do low contrast targets in comparison to high contrast targets.

(8). The wavelength and repetition rate of the laser pulses may interact with both the type and magnitude of damage elicited and these two factors should relate directly to changes in visual performance. All exposures to date have been made using the 532 nm line. In the next phase of the experiment we will begin exposing our animals to 1032 nm and combinations of both the visible and invisible lines.

(9). Multiple pulses should be more effective in producing shifts in visual performance than should single pulses of comparable total energy since multiple pulses are more apt to involve larger retinal areas due to eye movements. To date, our results have not confirmed this notion although we continue to explore the temporal consequences of repetitive exposures.

The methodology developed during a previous research project (39) and modified for the current effort appeared suitable for producing foveal exposures in awake, task oriented animals. This method allowed for the measurement of rhesus visual acuity during and immediately following laser exposure thereby allowing for the exploration of the effects of exposure energies at and below the ED_{50}. Over 90% of the exposures produced an immediate drop in visual sensitivity. The magnitude of this deficit was reminiscent of the maximum, permanent deficits observed in other studies where more intense irradiation was placed directly onto the fovea using anesthesia to limit eye and body movements. In those few cases where no immediate shift in acuity was observed for on-axis exposures, one might speculate that either involuntary or preinitiated voluntary eye movements resulted in irradiation of extrafoveal areas. The irradiation of these areas should produce little if any shift in maximal acuity since only foveal areas are normally involved in the detection of fine spatial detail. It is also possible that lid closures especially when subthreshold energy levels were employed might have resulted in reduced foveal involvement and hence produced only minimal shifts in visual acuity immediately following exposure.

Once exposed, our animals maintained vigil and continued to respond despite their often reduced visual sensitivity supporting the need for a task which requires the animal to maintain vigilance even while partially disabled. Further, our data suggest that our animals did not initially change their detection criterion (beta value) as indicated by their unchanged false alarm rate for targets below their new threshold level. What did change was the animal's sensitivity (d') to resolve this spatial task. The lack of a total functional impairment implies that the paradigm significantly motivated the animals to learn to employ unexposed retinal areas to make the required discrimination even if this meant looking off-axis at the critical features of the targets. For the single pulse condition using minimal diameter spots, this often meant "looking" around or through the minimally disrupted region of the fovea. While for the multiple pulse condition or for large diameter spots it would have meant that the animal must have employed regions outside the fovea for detection the critical feature of the target. The magnitude of the initial deficit and its dependence on beam diameter supports this parafoveal hypothesis.

The appropriateness of the rhesus as a human prototype is now well substantiated. The visual sensitivity of this species is essentially the same as that of the human observer. The achromatic acuity of the rhesus as measured in this study was similar to that of the human tested under similar viewing conditions. Some differences were

noted. For example, visual acuity of the rhesus was slightly superior to that of the human at minimal scotopic ranges and the human slightly superior to the rhesus within the photopic region. These minor differences can be explained by the slightly larger pupil diameter of the rhesus and the greater efficiency of its eyes to collect and absorb light. Also, the rhesus demonstrated a slightly reduced sensitivity to long wavelength light under maximum photopic conditions. This long wavelength insensitivity of the rhesus is similar to that observed in protanomalous human observers. While some correction factors might need to be applied when comparing the relative efficiencies of the normal human observer and the rhesus to absorb incident light, the perceptual consequences should to be remarkably similar.

The effects of eye movements and position has not be adequately explored. We have noted that relatively large deficits (50% to 90%) can be produced by even our minimal diameter beams (50 micron spot on the retina) when the exposure duration is set for 100 msec or when the animal receives multiple, brief exposures of sufficient power. While these brief durations prevented the animal from voluntarily moving his eye away from the bright light source they did not eliminate the rapid, irregular involuntary eye movements naturally occurring during any fixation. This type of eye movement smears any image across a larger retinal region than would be calculated purely on the basis of spot size. This might explain why even relatively small diameter retinal exposures (50 microns) produced a somewhat larger and longer decrement in postexposure visual acuity than might otherwise be expected.

Without eye movements or with shorter duration exposures one would not expect to observe any shift in postexposure acuity when minimal diameter (50 microns) exposures are used and such was the case even when the power density was above the ED_{50} level but exposure duration was limited to 15 nsec. In this study we have shown that with very short duration exposures (<50 msec) little or no observed temporary acuity deficits were observed regardless of the energy density employed. In those cases where the energy density was significantly above the ED_{50} level and when physical damage was likely but high restricted to a small retinal region one might expect the animal's performance to be more erratic as he must learn to "look" around damaged regions. This clearly was confirmed in our postexposure testing. Multiple exposures, on the other hand, that were either close or far in time from each other should eventually produce a consistent and long term drop in postexposure acuity as the lesion sites increasingly spread across the fovea. This too was confirmed in our initial investigations.

The notion that the region of retinal involvement, whether as the result of changes in beam diameter or exposure duration, has a significant effect on the magnitude and duration of any observed acuity deficit, was also supported by our off-axis experiments. Intentionally positioning the beam away from the animal's point of central fixation (off-axis) decreased both the magnitude and duration of any elicited acuity deficits. We have begun to measure baseline sensitivities of more peripheral regions of the retina by placing the exposing beam at various degrees of eccentricity.

For those foveal exposures which produced only transient changes in visual acuity, the duration for full photopic recovery was often significantly longer than that typically observed in human psychophysical studies where incoherent light produced a state of full beaching. The average recovery duration for our transient effect was 20 minutes and this time is much longer than the 3 to 5 min adaptation time characteristic of these types of photopic studies. This relatively long recovery time suggests that aberrant photochemical changes and/or neural processing within the fovea were operating which required a longer than usual time to reverse.

In those exposures where recovery was not complete within the 45 minute test session, partial recovery was often observed in subsequent postexposure sessions often days or even weeks following the initial exposure. These animals often experienced a greater deficit during the early stages of the recovery process which could have been the result of hemorrhages clouding the ocular media and edema altering photoreceptor orientations. As time passed, these physical alterations would naturally become reduced and so may partially explain the temporal changes observed in postexposure acuity measurements. The increased variability of performance following exposure might also

be explained by differential strategies used by the animal to employ unaffected retinal regions. As the animal learned to more consistently employ parafoveal regions near but not within the affected fovea, his visual performance should not only improve but also show less within and between session variability.

Our data again supports the notion that the nature of the visual task can significantly modify the magnitude of any performance changes following laser irradiation. Chromatic and low contrast targets appeared more affected by laser irradiation than did other types of visual displays. While these effects can be examined in postexposure assessments, unfortunately our procedure makes it more time consuming to study these effects for transient exposure conditions and for changes that might occur immediately following irradiation. Our methodology of exposing an animal only once per day and requiring the animal to maintain a stable acuity for at least 10 minutes at each condition limits the number of variables that can be studied in any one animal. Our animals typically are tested daily but their actual acuity testing does not extend beyond 45 minutes. Many of these variables will be studied during the final phase of this project.

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